

## AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of Claims:**

1-5. (cancelled)

6. (Currently Amended) A method of determining susceptibility to ~~bone~~bone mineral density (BMD)-independent fracture in a Caucasian female subject, the subject comprising:

(i) at least one estrogen receptor  $\alpha$  gene comprising a *Pvu*II site and a *Xba*I site, wherein the *Pvu*II site can exist as a P or p allelic form, and the *Xba*I site can exist as an X or x allelic form; and

(ii) a vitamin D receptor gene, wherein the vitamin D receptor gene comprises a *Bsm*I site, an *Apa*I site and a *Taq*I site, wherein the *Bsm*I site can exist as a B or b allelic form, the *Apa*I site can exist as an A or a allelic form, and the *Taq*I site can exist as a T or t allelic form,

said method comprising analyzing nucleic acid molecules obtained from the ~~mammalian~~ subject to determine which of the P, p, X, and x alleles of the estrogen receptor  $\alpha$  gene are present, and further comprising determining the copy number of a member of the group consisting of the P, p, X and x alleles of the estrogen receptor  $\alpha$  gene and the B, b, A, a, T and t alleles of the vitamin D receptor gene, wherein the presence of a haplotype comprising the p and x alleles of the estrogen receptor  $\alpha$  gene and a homozygous haplotype comprising the baT alleles of the vitamin D receptor gene is indicative of an increased susceptibility to ~~bone~~BMD-independent fracture and further comprising determining the copy number of a member of the group consisting of the P, p, X and x alleles of the estrogen receptor  $\alpha$  gene and the B, b, A, a, T and t alleles of the vitamin D receptor gene.

7. (cancelled)

8. (Previously presented) A method according to Claim 6, wherein said method is performed *in vitro*.

9. (Currently amended) A method according to claim 8, wherein said method is performed on a blood or tissue sample of ~~a~~the subject.

10. (Previously presented) The method of Claim 6 wherein the subject is suffering from low bone mineral density.

11. (Previously presented) The method of Claim 6 wherein the subject has a normal level of bone mineral density.

12. (Currently amended) A method of treating a Caucasian female subject to prevent or reduce the risk of ~~bone~~bone mineral density (BMD)-independent fracture, wherein the subject comprises:

(i) at least one estrogen receptor α gene comprising a *Pvu*II site and a *Xba*I site, wherein the *Pvu*II site can exist as a P or p allelic form, and the *Xba*I site can exist as an X or x allelic form; and

(ii) a vitamin D receptor gene, wherein the vitamin D receptor gene comprises a *Bsm*I site, an *Apa*I site and a *Taq*I site, wherein the *Bsm*I site can exist as a B or b allelic form, the *Apa*I site can exist as an A or a allelic form, and the *Taq*I site can exist as a T or t allelic form, wherein the presence of a haplotype comprising the p and x alleles of the estrogen receptor α gene and a homozygous haplotype comprising the baT alleles of the vitamin D receptor gene is indicative of an increased susceptibility to ~~bone~~bone-BMD-independent fracture,

said method comprising determining whether the px haplotype of the estrogen receptor α gene and the homozygous baT haplotype of the vitamin D receptor gene are present in said subject, and treating the subject to reduce the risk of ~~bone~~bone-BMD-independent fracture if the subject has both said haplotypes, wherein the treatment comprises at least one treatment selected from the group consisting of modifications to lifestyle, regular exercise, changes in diet and administration of a pharmaceutical preparation effective to prevent or reduce the risk of ~~bone~~bone-BMD-independent fracture.

13-20. (cancelled)

21. (Currently Amended) A method of formulating recommending a treatment regimen to decrease the risk of bone-bone mineral density (BMD)-independent fracture in a Caucasian female subject, wherein said subject comprises:

(i) at least one estrogen receptor  $\alpha$  gene comprising a *Pvu*II site and a *Xba*I site, wherein the *Pvu*II site can exist as a P or p allelic form, and the *Xba*I site can exist as an X or x allelic form; and

(ii) a vitamin D receptor gene, wherein the vitamin D receptor gene comprises a *Bsm*I site, an *Apal* site and a *Taq*I site, wherein the *Bsm*I site can exist as a B or b allelic form, the *Apal* site can exist as an A or a allelic form, and the *Taq*I site can exist as a T or t allelic form,

wherein the presence of a haplotype comprising the p and x alleles of the estrogen receptor  $\alpha$  gene and a homozygous haplotype comprising the baT alleles of the vitamin D receptor gene is indicative of an increased susceptibility to bone-BMD-independent fracture,

said method comprising analyzing nucleic acid molecules of the subject to determine whether both said haplotypes are present in said subject, and formulating recommending a treatment regimen when both said haplotypes are present in said subject, wherein the treatment regimen is effective to decrease the risk of bone-BMD-independent fracture if said haplotypes are present in said subject.

22-23. (cancelled)

24. (Currently amended) A method according to Claim 21, further comprising administering an appropriate treatment effective to decrease the risk of bone-BMD-independent fracture.

25-28. (cancelled)

29. (Previously presented) A method according to Claim 6, wherein the presence of the px haplotype is determined by amplification of a portion of the first intron of the estrogen receptor  $\alpha$  gene to yield an amplified fragment, followed by restriction enzyme digestion of the amplified fragment.

30. (Previously presented) A method according to Claim 6, wherein the presence of the baT haplotype of the vitamin D receptor gene is determined by amplification of a portion of the vitamin D receptor gene between exon 7 and the 3' untranslated region to yield an amplified fragment, followed by restriction enzyme digestion of the amplified fragment.

31-33. (cancelled)

34. (New) A method according to Claim 6, wherein the BMD-independent fracture is a vertebral fracture.

35. (New) A method according to Claim 12, wherein the BMD-independent fracture is a vertebral fracture.

36. (New) A method according to Claim 21, wherein the BMD-independent fracture is a vertebral fracture.